REMARKS

Status of the Claims

Claims 1-7, 9-24, and 26-29 are pending in the application. Claims 30-33 have been previously withdrawn from consideration and claims 1-29 have been examined. Claims 8 and 25 were previously canceled. Applicant hereby amends claims 1 and 23. After entry of this paper, claims 1-7, 9-24, and 26-29 remain pending for examination.

Amendments to the Claims

Applicant has amended claim 1. Support for the amendments to claim 1 is found at least at page 3, lines 15-16 and 24-26; page 19, line 21 to page 21, line 4; and page 33, line 28 to page 34, line 1; and original claim 8. Accordingly, the amendments to claim 1 add no new matter.

Applicant has amended claim 23. Support for the amendments to claim 23 is found at least at page 3, lines 15-16 and 24-26; page 19, line 21 to page 21, line 4; page 33, line 28 to page 34, line 1; and original claim 25. Accordingly, the amendments to claim 23 add no new matter.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-7, 9-24, and 26-29 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Specifically, the Office Action alleges that the phrase "the biological fragment" in claims 1 and 23 lack sufficient antecedent basis. Applicant has amended claims 1 and 23 to further clarify the antecedent basis of this phrase. Applicant thus respectfully requests reconsideration and withdrawal of the rejections of amended claims 1-7, 9-24, 26-29 under 35 U.S.C. §112, second paragraph.

Rejections Under 35 U.S.C §103

Claims 1-7, 11-17, 21-24, and 28-29 were rejected under U.S.C. §103 as allegedly obvious over U.S. Patent No. 6,017,693 to Yates, III et al. ("Yates") in view of U.S. Patent No. 5,710,713 to Wright ("Wright"), and the article *"Improving protein identification from peptide mass fingerprinting through a parameterized multi-level scoring algorithm and optimized peak detection"* in Electrophoresis 1999, Volume 20, pages 3535-3550 by Gras et al. ("Gras"), (collectively "the cited references").

Applicant believes that original claims 8 and 25 were considered allowable as no rejection was applied to these claims in the Office Action of January 12, 2004; the last Office Action in which these claims were pending for examination. In Applicant's previous response, Applicant amended claims 1 and 23 to incorporate the limitations, respectively, of claims 8 and 25. The Final Action, however, did not consider these amendments to place the claims in condition for allowance, stating at page 9 that:

> While some of the claim limitations of cancelled claims 8 and 25 have been amended into claims 1 and 23, not all of the limitations of cancelled claims 8 and 25 (i.e. separate determining steps) have been amended into claims 1 and 23.

Although Applicant disagrees with the Final Action, Applicant nevertheless has amended claims 1 and 23 to more literally incorporate the language, respectively, of claims 8 and 25 into these claims. Therefore, Applicant submits that amended claims 1 and 23, and claims 2-7, 9-22, 24 and 26-29 that depend therefrom, are in condition for allowance.

Although Applicant believes that amended claims 1 and 23 are in condition for allowance, Applicant wishes to address for the record certain positions in the Final Action. Specifically, the Final Action alleges that Applicant has not argued the 103 rejection beyond the argument regarding the phrases "determining a biomolecule fragment score" using "the mass signal intensity for said mass signal, a biomolecule fragment detection parameter...and a mass error for said mass signal".

Applicant must respectfully disagree with this characterization of Applicant's argument to the extent that it suggests Applicant has not responded to the rejection under 35 U.S.C. §103. Applicant has submitted in his prior responses and again submits evidence why the cited

references, either alone or in proper combination, fail to teach or suggest all elements of Applicant's claims, or these claims as a whole. Specifically, Applicant has shown that the cited references do not teach or suggest "determining a biomolecule fragment score" of a mass signal using, *inter alia*, a mass signal intensity, a biomolecule fragment detection parameter, and a mass error for the mass signal, as set forth in Applicant's claims.

As Applicant has set forth in prior responses, the specification makes clear that a biomolecule fragment detection parameter, as set forth in amended claims 1 and 23, reflects the general relative mass signal intensity relationships that arise from differences in the likelihood of detecting different biomolecule fragments as a mass signal in the mass spectrum of the sample. For example, the specification at page 21, line 21, to page 30, line 20, makes clear to one of ordinary skill in the art that,

> An underlying principal to determining a biomolecule fragment parameter is that the numerical values of the parameters reflect the general relative mass signal intensity relationships between biomolecule fragments, and/or the fraction of a biomolecule fragment generally observed, in a mass spectrum of the sample or related samples that arise from differences in biomolecule fragment sequence and chemistry of the biomolecule fragmentation and/or digestion...

(emphasis added). None of the cited references teach or suggest a biomolecule fragment detection parameter based, at least in part, on relative mass signal intensity relationships between biomolecule fragments (and/or fractions thereof); and the Final Action points to no portions of the cited references that do so. Rather, the entire basis for the Final Action's assertion that the cited references teach or suggest a biomolecule fragment detection parameter (as set forth in Applicant's claims) is based on Yates' use of a mass tolerance, stating at page 4 in the Final Action that,

> Yates III et al. describe a mass tolerance of the unknown peptide from which spectra from known sequences (i.e. potential source biomolecules) are identified if they fall within this tolerance amount...which is reasonably interpreted as the biomolecule fragment detection parameter.

(emphasis added).

Applicant again must respectfully disagree. "Mass tolerance" cannot be reasonably interpreted to be a "biomolecule fragment detection parameter," as set forth in Applicant's claims because, *inter alia*, the "mass tolerance" quantity of Yates is in no way determined

using, even in part, relative mass signal intensity relationships between biomolecule fragments (and/or fractions thereof). Instead, the quantity of Yates equated by the Final Action with Applicants "biomolecule fragment detection parameter," -i.e., Yates' mass tolerance- is a measure based on the mass difference between a measured and predicted mass signal.

Specifically, Yates at column 4, line 59 to page 5, line 8, reads:

> In order to generate predicted mass spectra from a protein sequence library, according to the process of FIG. 3, sub-sequences within each protein sequence are identified which have a mass which is within a tolerance amount of the mass of the unknown peptide. As noted above, the mass of the unknown peptide is known from the tandem mass spectrometer 34. Identification of candidate sub-sequences 34 is shown in greater detail in FIG. 4. In general, the process of identifying candidate sub-sequences involves summing the masses of linear amino acid sequences until the sum is either within a tolerance of the mass of the unknown peptide (the "target" mass) or has exceeded the target mass (plus tolerance). If the mass of the sequence is within tolerance of the target mass, the sequence is marked as a candidate. If the mass of the linear sequence exceeds the mass of the unknown peptide, then the algorithm is repeated, beginning with the next amino acid position in the sequence.

Thus, the term "mass tolerance", as taught by Yates, is a mass difference between the molecular weight of the unknown peptide and a predicted sequence.

It is elementary in the field of mass spectrometric analysis that a mass difference (or a mass error) between mass signals (either measured, predicted or both) is distinctly different from and not equatable with the signal intensity associated with a mass signal. A simple glance at a typical mass spectrum with the x-axis representing mass and the y-axis representing intensity is a plain example that intensity and mass are two distinct physical quantities. Further, a comparison of the physical units associated with mass (e.g., the kilogram) and intensity (ultimately related to current, e.g. the amp, as detection is typically done electronically) shows that mass cannot reasonably be interpreted as intensity or even its equivalent in the present application or the field of mass spectrometric analysis. Accordingly, a "mass tolerance" as taught by Yates cannot be interpreted as a "biomolecule fragment detection parameter" as that term is used in Applicant's claims. Applicant thus submits that Yates does not teach or suggest a "biomolecule fragment detection parameter" or its use as set forth in either amended independent claim 1 or 23.

Applicant further submits that Wright and Gras, either alone or in proper combination, does not provide this teaching missing in Yates; and the Final Action does not appear to assert otherwise. Specifically, the Final Action points to no portion of either Wright or Gras as teaching or suggesting, either alone or in combination with each other and/or Yates, a "biomolecule fragment detection parameter" or its use as set forth in either amended independent claim 1 or 23. Therefore, Applicant respectfully submits that amended claims 1 and 23, and claims 2-7, 9-22, 24 and 26-29 that depend therefrom, are novel and non-obvious over Yates, Wright, and Gras, either alone or in combination.

As, the phrase "determining a biomolecule fragment score" is a specific step of Applicant's method claims and therefore a limitation thereof that must be taught by the cited references to render Applicant's claims obvious. The object determined "a biomolecule fragment score" is further limited in Applicant's amended claims as being determined from, *inter alia*, "said biomolecule fragment detection parameter ... for said mass signal." and the biomolecule fragment detection parameter is based, at least in part, on relative mass signal intensity relationships between biomolecule fragments (and/or fractions thereof). Accordingly, as the Final Action has failed to show where the cited references teach or suggest determining a biomolecule fragment detection parameter using at least in part relative mass signal intensity relationships of any kind, Applicant also submits that the Final Action has failed to establish a *prima facie* case of obviousness against Applicant's claims.

CONCLUSION

In view of the above, it is believed that all presently pending claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone call would expedite the prosecution of this case, the Examiner is invited to call the undersigned at (617) 994-0829.

Applicant believes that no additional fee is due with this amendment and Reply. However, if any additional fee is due, please charge our Deposit Account 12-0080, under Order No. SY9-155 from which the undersigned is authorized to draw.

Dated: March 16, 2005

Respectfully submitted,

By _____

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